

IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (Currently Amended) Process for preparing cephradine, said process comprising reacting 7- aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DHa) in the presence of an enzyme in a reaction mixture to form cephradine, resulting in a conversion of 7-ADCA into cephradine of at least 70 %, wherein the concentration D-dihydrophenylglycine (DH) in the reaction mixture is below 2wt. %;

wherein throughout the reaction if said enzyme is a wild type penicillin acylase said reacting is carried out at a temperature below 15°C, or if said enzyme is an acylase having a higher S/H ratio than the wild type acylase of E.coli throughout the reacting step said reacting is carried out at a temperature of at least 15°C.

2. (Currently Amended) Process according to claim 1, wherein said reacting results in a conversion of 7-ADCA into cephradine of at least 80%, ~~preferably at least 90%.~~

3. (Currently Amended) Process according to claim 1, wherein said reacting results in a conversion of D-dihydrophenylglycine in activated form (DHa) into cephradine (CEF) of at least 70%, ~~preferably at least 80%, more preferably at least 90%,~~ wherein

the conversion of DHa into CEF = $(n_{\text{CEF}} / n_{\text{DHa}}) * 100\%$;

n_{CEF} = quantity of cephradine formed (in mole); and

n_{DHa} = total quantity of DHa added to reaction mixture (in mole).

4. (Currently Amended) Process according to claim 1, wherein the concentration DH in the reaction mixture is maintained below 2 wt. %, ~~preferably below 1 wt. %~~ throughout said reacting by controlling the pH of the reaction mixture between pH 6 and 9 and/or ~~the temperature~~ when said enzyme is a wild type penicillin acylase said reacting is carried out at a temperature between -5 and 15°C, or when said enzyme is an acylase

having a higher S/H ratio than the wild type acylase of E.coli said reacting is carried out at a temperature of between 15 and 35°C.

5. (Currently Amended) Process according to claim 1, wherein the sum of the quantity of 7-ADCA added to the reaction mixture and DHa added to the reaction mixture is between 10 and 2000 mmol per liter of reaction mixture, ~~preferably between 50 and 1500 mmole per liter of reaction mixture.~~

6. (Currently Amended) Process according to claim 1, ~~characterised~~ characterized in that dihydrophenylglycine in activated form is dihydrophenylglycine methylester.

7. (Currently Amended) Process according to claim 1, ~~characterised~~ characterized in that dihydrophenylglycine in activated form is a HCl salt of dihydrophenylglycine methylester.

Claims 8-10 (canceled)

11. (Currently Amended) Process according to claim 1, ~~characterised~~ characterized in that the enzyme is ~~immobilised~~ immobilized on a carrier.

12. (Previously Presented) Process according to claim 1, wherein the process is a batch process.

Claims 13-14 (Canceled)

15. (Currently Amended) Process according to ~~claim 14~~ claim 1, wherein said reacting is carried out at a pH of at least 7.0.

Claim 16 (Canceled)

17. (Currently Amended) Process according to ~~claim 16~~ claim 1, wherein said reacting is carried out at a pH of below 7.7.

18. (Currently Amended) Process according to ~~claim 16~~ claim 1, ~~characterised~~ characterized in that the enzyme is a mutant penicillin acylase is derived from a wild type acylase via recombinant DNA methodology by substituting one amino acid residue for a new residue.

19. (Currently Amended) Process according to claim 1, wherein the process comprises ~~crystallising~~ crystallizing the cephradine from an aqueous solution to form cephradine hydrate.

20. (Currently Amended) Process, ~~preferably~~ according to claim 19, said process comprising:

reacting aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DHa) in the presence of an enzyme in a reaction mixture to form cephradine; and

~~crystallising~~ crystallizing the cephradine from an aqueous solution, in which aqueous solution the ratio $m_{\text{CEF}} / (m_{7\text{-ADCA}} + m_{\text{CEF}}) > 0.7$, preferably > 0.8 , more preferably > 0.9 , and wherein $X_{\text{DH}} = 0\text{-}2 \text{ wt. \%}$, preferably $0\text{-}1 \text{ wt. \%}$, wherein

m_{CEF} = molar quantity of cephradine in the aqueous solution;

$m_{7\text{-ADCA}}$ = molar quantity of 7-ADCA in the aqueous solution; and

X_{DH} = concentration of DH in the aqueous solution relative to the total weight of the aqueous solution.

21. (Currently Amended) Process according to claim 19, wherein the process comprises separating the enzyme from the cephradine prior to said ~~crystallising~~ crystallizing.

22. (Currently Amended) Process according to claim 1, wherein the concentration 7-ADCA in the aqueous solution is between 0 and 5 wt. %, ~~preferably between 0 and 2 wt. %.~~

23. (Currently Amended) Process according to claim 19, wherein said ~~crystallising~~ crystallizing is performed at a temperature of between 45 and 60 °C, ~~preferably between 48 and 55 °C.~~

24. (Currently Amended) Process for preparing cephadrine hydrate crystals, ~~characterised~~ characterized in that the process comprises ~~crystallising~~ crystallizing cephadrine from an aqueous solution to form cephadrine hydrate, wherein said ~~crystallising~~ crystallizing is carried out at a temperature of between 45 and 60°C, ~~preferably between 48 and 55°C.~~

25. (Currently Amended) Process according to claim 19, wherein said ~~crystallising~~ crystallizing is performed at a pH of between 4.0 and 6.0, ~~preferably at a pH of between 4.5 and 5.5.~~

26. (Currently Amended) Process for the preparation of cephadrine ~~characterised~~ characterized in that the process comprises:

- reacting 7-aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form in the presence of an enzyme in a reaction mixture to prepare cephadrine; and
- ~~crystallising~~ crystallizing the cephadrine from an aqueous solution to form cephadrine hydrate according to the process according to claim 24.

27. (Currently Amended) Process according to claim 1, wherein part of the cephadrine formed is crystallized and present in the reaction mixture as cephadrine hydrate, and wherein the process further comprises dissolving at least part of said cephadrine hydrate in said reaction mixture.

28. (Currently Amended) Process according to claim 27, wherein said dissolving is effected at a pH of above 8, ~~preferably at a pH of between 8.5 and 9.~~

29. (Currently Amended) Process according to claim 19, ~~characterised~~ characterized in that said ~~crystallising~~ crystallizing is performed at such pH and at such temperature that the absorbance at 450 nm of the cephradine hydrate prepared is below 0.050.

30. (Currently Amended) Process according to claim 1 ~~characterised~~ characterized in that said reacting is carried out in the presence of sodium bisulphite.

Claims 31-32 (Canceled).